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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/897,583      | 06/29/2001  | Thomas A. Szyperski  | 19226/2051 (R-5655) | 1224             |

7590 10/19/2004

Michael L. Goldman  
NIXON PEABODY LLP  
Clinton Square  
P.O. Box 31051  
Rochester, NY 14603

EXAMINER

GAKH, YELENA G

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1743

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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|                              |  |   |  |
|------------------------------|--|---|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>09/897,583     | <b>Applicant(s)</b><br>SZYPERSKI, THOMAS A. |  |
|                              | <b>Examiner</b><br>Yelena G. Gakh, Ph.D. | <b>Art Unit</b><br>1743                     |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 August 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-132 is/are pending in the application.
- 4a) Of the above claim(s) 1-90 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 91-132 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>06/10/04</u>  | 6) <input type="checkbox"/> Other: _____                                    |

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### DETAILED ACTION

1. Amendment filed on 08/20/04 is acknowledged. Claims 1-132 are pending in the application. Claims 1-90 are withdrawn from consideration. Claims 91-132 are examined on merits.

#### *Response to Amendment*

2. In the response to the amendment the examiner withdraws rejection of claim 91-132 under 35 U.S.C. 112, first paragraph and objections to the drawings. The rejection over the prior art stands as it was established in the previous Office action.

#### *Claim Rejections - 35 USC § 103*

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. **Claims 91-102, 131 and 132** are rejected under 35 U.S.C. 103(a) as being unpatentable over Szyperski et al. (J. Biomol. NMR, 1998, IDS) in view of Fernandez et al. (J. Biomol., 1998) or Gehring et al. (JMR, 1998) and Yamazaki et al. (JACS, 1993).

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Szyperski discloses “sequential resonance assignment of medium sized  $^{15}\text{N}/^{13}\text{C}$ -labeled proteins with projected 4D triple resonance NMR experiments” (Title), comprising performing 3D  $\text{H}^{\alpha\beta}\text{C}^{\alpha\beta}(\text{CO})\text{NHN}$  experiment, 3D  $\text{HNNCAHA}$  experiment and 3D  $\text{HNN}\langle\text{CO},\text{CA}\rangle$  experiment for assigning corresponding chemical shifts for the protein backbone.

Szyperski does not specifically disclose using 3D  $\text{HCCH-COSY}$  and 2D  $\text{HBCB}(\text{CGCD})\text{HD}$  NMR experiments for assigning aliphatic and aromatic side chain chemical shifts.

Fernandez and Gehring disclose side chain assignments based on 2D and 3D  $\text{HCCH-COSY}$  NMR techniques for assignment of aliphatic side chain chemical shifts for proteins, while Yamazaki teaches 2D RD  $\text{HBCB}(\text{CGCD})\text{HD}$  NMR technique for assigning aromatic side chain chemical shifts.

It would have been obvious for anyone of ordinary skill in the art to add two NMR techniques disclosed by Fernandez or Gehring and Yamazaki to the strategy disclosed by Szyperski in order to perform more complete assignment of signals in NMR spectra of proteins by adding assignments for the side chains (aliphatic and aromatic) to the assignment of the protein backbone.

6. **Claims 103-130** are rejected under 35 U.S.C. 103(a) as being unpatentable over Szyperski in view of Fernandez or Gehring and Yamazaki, as applied to claims 91-102, 131 and 132 above, and further in view of Shirra (“Three Dimensional NMR Spectroscopy”, November 28, 1996) or “Cell Cycle/Gene Regulation” protocol, 1998).

Szyperski in view of Fernandez or Gehring and Yamazaki do not specifically disclose some other 3D experiments recited in claims 103-130 for assigning chemical shifts of various backbone and side-chain nuclei of proteins.

Shirra and “Cell Cycle” protocol describe various 3D and 2D experiments for assigning chemical shifts of various nuclei in backbone and side chains of proteins via different pathways, the combination of which leads to complete assignment of NMR spectra, as well as determining protein structure from corresponding NOESY experiments.

It would have been obvious for anyone of ordinary skill in the art to combine various experiments listed in Shirra or “Cell Cycle” protocol, or to modify them in the same way as taught by Szyperski for pulse sequences disclosed by Szyperski in view of Fernandez or Gehring

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and Yamazaki in order to obtain completely assigned NMR spectra and to determine tertiary structure of proteins from NOE data, since these are the main goals of the cited papers.

### ***Response to Arguments***

7. Applicant's arguments filed 08/20/04 have been fully considered but they are not persuasive. While the examiner agrees with the Applicant's statements regarding importance of full assignment of protein NMR spectra for analysis of protein structures, she cannot agree with non-obviousness of the method for such assignment disclosed in the instant application. Advantages of reduced dimensionality (RD) of triple-resonance (TR) experiments, specifically  $3D\ H^{\alpha/\beta}\ C^{\alpha/\beta}(CO)NHN$ ,  $3D\ HNNCAHA$ , and  $3D\ HNN<CO,CA>$  experiments are unambiguously demonstrated in the Applicant's own paper of 1998. Experiments disclosed by Fernandez, Gehring, Yamazaki and Shirra are complimentary to Szyperski's sequences for full assignment of protein NMR spectra. Modifying these experiments the way disclosed by Szyperski in order to combine advantages of higher resolution multi-dimensional NMR and higher sensitivity and efficiency of NMR spectra of lower dimensionality would have been obvious for any routineer of the art in view of Szyperski's disclosure. In the Applicant's argumentation there is a tendency to treat each reference individually. The rejection is established on combination of references. The examiner did not find convincing arguments regarding non-obviousness of modifying experiments taught by Fernandez, Gehring, Yamazaki and Shirra the way disclosed by Szyperski, especially since all experiments create the same conditions used by Szyperski, i.e. "a cosine-modulation of the transfer amplitude, yielding peak doublets encoding  $n$  chemical shifts in a  $n-1$  dimensional spectrum" (Szyperski, 1998, page 141).

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yelena G. Gakh  
10/16/04

Handwritten signature of Yelena G. Gakh in black ink.